

A 3D Tissue-Printing Approach for Validation of Diffusion Tensor Imaging in Skeletal Muscle.

Journal: Tissue Eng Part A

Publication Year: 2017

Authors: David B Berry, Shangting You, John Warner, Lawrence R Frank, Shaochen Chen, Samuel R Ward

PubMed link: 28338417

Funding Grants: Development of 3D Bioprinting Techniques using Human Embryonic Stem Cells Derived Cardiomyocytes for Cardiac Tissue Engineering

Public Summary:

The focus of this study employs new 3D printing strategies to develop a novel set of precision-engineered phantoms for characterizing the interrelationship between microstructural variables and magnetic resonance -diffusion parameters in skeletal muscle. We hypothesize that physiologically relevant changes in muscle microstructure and microfluidics are separable and can be specifically identified using a novel application of multi-echo diffusion tensor magnetic resonance imaging experiments. We used 50%PEGDA/50%PBS and 80%PEGDA/20%PBS prepolymer solutions to successfully fabricate the five geometric designs (30µm hexagons, 50µm hexagons, and 70µm hexagons 50µm hexagon phantoms with 40% of walls randomly deleted, and phantoms with no geometry) and the two histology informed designs (control and 30-day denervation). Qualitatively, the five printed designs mimicked the input designs well based on microscopic image examination. These microscopic images demonstrate the use of rapid 3D printing technology to fabricate phantoms of muscle tissue that reproduce the features of each muscle fiber.

Scientific Abstract:

The ability to noninvasively assess skeletal muscle microstructure, which predicts function and disease, would be of significant clinical value. One method that holds this promise is diffusion tensor magnetic resonance imaging (DT-MRI), which is sensitive to the microscopic diffusion of water within tissues and has become ubiquitous in neuroimaging as a way of assessing neuronal structure and damage. However, its application to the assessment of changes in muscle microstructure associated with injury, pathology, or age remains poorly defined, because it is difficult to precisely control muscle microstructural features in vivo. However, recent advances in additive manufacturing technologies allow precision-engineered diffusion phantoms with histology informed skeletal muscle geometry to be manufactured. Therefore, the goal of this study was to develop skeletal muscle phantoms at relevant size scales to relate microstructural features to MRI-based diffusion measurements. A digital light projection based rapid 3D printing method was used to fabricate polyethylene glycol diacrylate based diffusion phantoms with (1) idealized muscle geometry (no geometry; fiber sizes of 30, 50, or 70 µm or fiber size of 50 µm with 40% of walls randomly deleted) or (2) histology-based geometry (normal and after 30-days of denervation) containing 20% or 50% phosphate-buffered saline (PBS). Mean absolute percent error (8%) of the printed phantoms indicated high conformity to templates when "fibers" were >50 µm. A multiple spin-echo echo planar imaging diffusion sequence, capable of acquiring diffusion weighted data at several echo times, was used in an attempt to combine relaxometry and diffusion techniques with the goal of separating intracellular and extracellular diffusion signals. When fiber size increased (30-70 µm) in the 20% PBS phantom, fractional anisotropy (FA) decreased (0.32-0.26) and mean diffusivity (MD) increased (0.44×10^{-3} mm²/s- 0.70×10^{-3} mm²/s). Similarly, when fiber size increased from 30 to 70 µm in the 50% PBS diffusion phantoms, a small change in FA was observed (0.18-0.22), but MD increased from 0.86×10^{-3} mm²/s to 1.79×10^{-3} mm²/s. This study demonstrates a novel application of tissue engineering to understand complex diffusion signals in skeletal muscle. Through this work, we have also demonstrated the feasibility of 3D printing for skeletal muscle with relevant matrix geometries and physiologically relevant tissue characteristics.